

AMENDMENTS TO THE SPECIFICATION

Please replace the paragraph beginning at page 1, line 6, with the following re-written paragraph:

-- This application is a continuation of Application No. 09/361,026, filed July 23, 1999, now U.S. Patent 6,699,497, granted March 2, 2004, which Claims the benefit of U.S. Provisional Application Serial No. 60/094,059 filed July 24, 1998, both of which are incorporated herein by reference. --

Please replace the paragraph beginning at page 8, line 1, with the following re-written paragraph:

-- As used herein, the phrase "predetermined area of skin" intends a defined area of intact ~~unbroken~~ skin or ~~mucosal~~ tissue. That area will usually be in the range of about 5 cm² to about 100 cm². --

Please replace the paragraph beginning at page 8, line 28, with the following re-written paragraph:

-- As used herein, the term "transdermal" intends ~~both percutaneous and transmucosal administration, i.e., passage of fenoldopam through a body surface or membrane such as intact unbroken skin or mucosal tissue~~ passage of fenoldopam through the skin into the systemic circulation. --

Please replace the paragraph beginning at page 10, line 7, with the following re-written paragraph:

-- (c) means for maintaining the reservoir in fenoldopam transmitting relation with a ~~body surface or membrane~~ the skin, wherein a therapeutically effective amount of fenoldopam is delivered at a therapeutically effective rate during an administration period in order to achieve and maintain therapeutic blood or plasma levels throughout a substantial portion of the administration period. --

Please replace the paragraph beginning at page 12, line 8, with the following re-written paragraph:

-- This invention finds particular usefulness in administering fenoldopam across skin. ~~It is also useful, however, in administering fenoldopam across mucosa.~~ According to the invention, fenoldopam is placed in fenoldopam transmitting relationship to ~~an appropriate body surface~~ the skin, preferably in a pharmaceutically acceptable carrier thereof, and maintained in place for the desired administration period. --

Please replace the paragraph beginning at page 12, line 14, with the following re-written paragraph:

-- The fenoldopam and permeation enhancer are typically dispersed within a physiologically compatible matrix or carrier, as more fully described below, which may be applied directly to the body as an ointment, gel or cream, ~~cream,~~ ~~suppository or sublingual or buccal tablet~~. When used in the form of a liquid, ointment, lotion, cream or gel applied directly to the skin, it is preferable, although not required, to occlude the site of administration. Such compositions can also contain other permeation enhancers, stabilizers, dyes, diluents, pigments, vehicles, inert fillers, anti-irritants, excipients, gelling agents, vasoconstrictors, vasodilators, and other components of topical compositions as are known to the art. --

Please replace the paragraph beginning at page 16, line 8, with the following re-written paragraph:

-- Fenoldopam can be administered to human skin ~~or mucosa~~ by direct application to the skin ~~or mucosa~~ in the form of an ointment, gel, cream or lotion, for example, but are preferably administered from a skin patch or other known transdermal delivery device which contains a saturated or unsaturated formulation of the fenoldopam and enhancer. The formulation may be aqueous or non-aqueous. The formulation should be designed to deliver the fenoldopam and any anti-irritant and/or enhancer at the necessary fluxes. Aqueous formulations typically comprise water or water/ethanol and about 1-5 wt% of a gelling agent, an example being a hydrophilic polymer such as hydroxyethylcellulose or hydroxypropylcellulose. When using aqueous formulations, it is preferable to maintain the pH at less than about 5.5, more preferably between about pH 2 - 4.5 in order to provide a stable fenoldopam

formulation. Typical non-aqueous gels are comprised of silicone fluid or mineral oil. Mineral oil-based gels also typically contain 1-2 wt% of a gelling agent such as colloidal silicon dioxide. The suitability of a particular gel depends upon the compatibility of its constituents with the fenoldopam, anti-irritant, and the permeation enhancer in addition to any other components in the formulation. --

Please replace the paragraph beginning at page 17, line 7, with the following re-written paragraph:

-- The amount of fenoldopam present in the therapeutic device and required to achieve an effective therapeutic result depends on many factors, such as the minimum necessary dosage of the fenoldopam for the particular indication being treated; the solubility and permeability of the matrix, taking into account the presence of permeation enhancer, of the adhesive layer and of the rate-controlling membrane, if present; and the period of time for which the device will be fixed to the skin. The minimum amount of fenoldopam is determined by the requirement that sufficient quantities of fenoldopam must be present in the device to maintain the desired rate of release over the given period of application. ~~The maximum amount for safety purposes is determined by the requirement that the quantity of fenoldopam present must not support a rate of release that reaches toxic levels.~~ --

Please replace the paragraph beginning at page 17, line 7, with the following re-written paragraph:

-- The fenoldopam may be present in the matrix or carrier at a concentration at or below saturation. An excess amount of fenoldopam above saturation may be included in the matrix or carrier, the amount of excess being a function of the desired length of the delivery period of the system. Fenoldopam may be present at a level below saturation without departing from this invention as long as it is continuously administered to the skin ~~or mucosal~~ site at a therapeutic rate and for a period of time sufficient to deliver a therapeutically effective amount of fenoldopam that provides the desired therapeutic result. --